REMARKS

Claims 22-24 and 29-40 are under examination and have been rejected.

Withdrawn Claim

Based on Applicants' election of the invention of Group II (claims 22-24), the Examiner has withdrawn from consideration all the remaining claims. Applicants had also, by Preliminary Amendment, added claims 28-40. The Examiner has withdrawn claim 28 on grounds that it changes the scope of claim 22.

In response, Applicants respectfully contend that this is not appropriate because claim 28 depends from claim 22 and simply recites an additional limitation. Because claim 22 recites the word "comprising" the possibility of additional components of the recited composition are certainly contemplated and the scope should not be considered different simply because Applicants have named a particular additional component. If claim 28 had offered the possibility of substituting an anti-bacterial antibody for the anti-viral antibody used in claim 22, then the scope might be different but simply adding an additional component is already within the scope of the claim because of the "comprising" language. Consequently, Applicants believe that claim 28 merely limits, but does not change, the scope of claim 22 and therefore request that claim 28 be rejoined with the others for examination purposes.

In sum, if claim 22 is allowable then claim 28 is allowable as well.

Rejection Under 35 U.S.C. 102(b)

Claim 24 was rejected under 35 U.S.C. 102(b) as anticipated by Johnson et al

(1999), which teaches the *in vivo* efficacy of MEDI-493 in the clinical treatment of RSV infection.

In response, Applicants note that it is established Patent Law that "Under 35 U.S.C. §102, anticipation requires that each and every element of the claimed invention be disclosed in the prior art. . . . In addition, the prior art reference must be enabling, thus placing the allegedly disclosed matter in the possession of the public." (see: *Akzo N.V. v. United States International Trade Commission*, 1 USPQ 2d 1241, 1245 (Fed. Cir. 1986), *cert. denied*, 482 U.S. 909 (1987).

In addition, "Anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, *arranged as in the claim*." See: *Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co.*, 221 USPQ 481, 485 (Fed. Cir. 1984) (emphasis added).

Finally, "From the evidence available to it, the initial burden of making out a prima facie case of prior invention is on the Patent Office. . . . When the Patent Office has made out a prima facie case of priority the burden would then shift to the applicant to rebut it." See: *In re Bass*, 177 USPQ 178, 186 (C.C.P.A. 1973)

In sum, "A prior art reference anticipates a claim only if the reference discloses, either expressly or inherently, every limitation of the claim. . . . "'[A]bsence from the reference of any claimed element negates anticipation.'" See: *Row v. Dror*, 42 USPQ 2d 1550, 1553 (Fed. Cir. 1997) (quoting *Kloster Speedsteel AB v. Crucible, Inc.*, 230 USPQ 81, 84 (Fed. Cir. 1986))

Here, Applicants respectfully contend that the Examiner has merely cited a reference that uses MEDI-493 as an anti-viral agent but that does not disclose use of a composition comprising both antibody and anti-inflammatory agent for that use. Claim 24 depends from claim 22 and thus recites all limitations of that claim, including use of

a composition of the recited agents and not just one of them. It is the same as if claim 24 recited use of a composition of antibody and anti-inflammatory agent wherein "MEDI-493" replaces the term "anti-viral neutralizing antibody" in claim 22 but all limitations of claim 22 would be present and neither the Examiner, nor the reference, accounts for these. Nor does Johnson et al enable use of such a composition because the reference makes no mention of anti-inflammatory agents. Consequently, Johnson does not anticipate claim 24.

Claims 22, 23, 29-34 and 36-40 were rejected under 35 U.S.C. 102(b) as anticipated by Prince et al (U.S. Pat. No. 5,290,540), which teaches *in vivo* treatment of a respiratory disease using an antibody and anti-inflammatory agent.

In response, claim 22 has been amended to recite the composition of claim 1 using an anti-viral neutralizing antibody and to state that such composition is administered systemically (as supported in the application as filed, at page 12, line 8, at page 24, lines 18-19, at page 26, lines 27-28, and at page 28, lines 23-26, among other instances). In addition, claim 31, directed to use of a regimen of both anti-viral and anti-inflammatory agents, has been similarly amended.

Conversely, the disclosure of the Prince '540 patent is limited to topical administration of an anti-inflammatory agent (see first sentence in the Abstract of the '540, as well as at column 10, lines 33-34, stating that all regimens were administered topically). Thus, the Prince et al '540 patent does not anticipate the claims of the invention.

Further, Applicants reiterate the above-arguments regarding anticipation based on the Johnson reference.

Rejection Under 35 U.S.C. 103(a)

Claim 35 was rejected under 35 U.S.C. 103(a) as being unpatentable over Prince et al (U.S. Pat. No. 5,290,540) in view of Johnson et al (1999), on grounds that Prince teaches the superiority of combining administered anti-viral and anti-inflammatory agents to accelerate clinical therapy.

Because claim 35 is directed to MEDI-493 but depends from claim 31, it contains all the limitations of claim 31 so that Applicants contend that the combination of these references does not render claim 35 obvious.

Initially, Applicants note that claim 31 has been amended to recite that the regimen, containing the anti-viral antibody and the anti-inflammatory agent, is administered systemically.

This is an important advance in view of Prince et al (2000 - reference K1 of Applicants' Form 1449 submission), which states that the '540 patent (ref. 21 in said paper) was directed to topical applications (see page 1330, column 1, first sentence of last paragraph) whereas systemic applications were found to be useful in these new results - but not common – and expressing doubt that those in the art would be receptive to such systemic use, thereby necessitating further experimentation. Conversely, the applications of the examples provided by Applicants represent mostly systemic administration of both antibody and anti-inflammatory agents, most of which examples were also disclosed in Application Serial No. 60/201,404, filed 3 May 2000, which is the priority application claimed by the present case.

The Prince et al paper was published electronically on 9 October 2000 (see footnote on page 1326 thereof), well after Applicants' priority date. Thus, at the time of Applicants' priority date, because there would have been reluctance in the art to use systemic administration, for example, of triamcinolone, further experiments were

undertaken using other anti-inflammatory agents, such as methyl prednisolone and dexamethasone. Applicants call the Examiner's attention to the fact that these are described in the examples of the application.

In addition, Applicants note in the application (page 2, lines 20-23) that treatment of RSV with steroids was shown in some cases to have little effect when administered systemically rather than topically, whereas Applicants' methodology shows them to have a greater effect when administered systemically if done along with a potent neutralizing antibody.

In addition, there are some unexpected results for Applicants' methodology. Thus, Figure 4 of the Application (Page 7, line 28, over to page 8, line 3) shows the results of antibody/steroid combination therapy on RSV pneumonia in cotton rats as described in Example 2. Panel A shows the results for virus titer for groups 1-3, panel B shows the results for virus titer for groups 4-6, and panel C shows the results for composite pathology score. These data indicate a lack of rebound pathology following systemic combination therapy whereas rebound pathology was a problem with topical administration. Such rebound pathology was found to be a problem for earlier work by Prince et al (2000), at page 1328, column 2, lines 5-10.

As taught by Applicants (see Page 21, line 27, over to page 22, line 3 of the application), one of the innovations of the invention is the ability to provide effective treatment of diseases, such as RSV, pneumonia, and other viral diseases, such as influenza and disease caused by PIV, by systemic treatment.

The rejection based on obviousness is directed to the combination of the Johnson paper with the '540 patent of Prince (both of whom are the inventors of the present application) but Applicants contend that there would have been no motivation to combine these references because Prince (the '540) shows topical

application of the anti-inflammatory agent while Johnson et al teach intramuscular administration (i.e., systemic) of MEDI-493. Consequently, those skilled in the art would not have thought to combine these references because, prior to the Prince et al (2000) paper, those in the art would not have been motivated to administer the anti-inflammatory agent systemically regardless of how the anti-viral agent is administered. Thus, with no motivation (even reluctance) to combine these references, they fail to render the claimed invention (claim 35) obvious.

In support of this lack of motivation (even reluctance) to combine, Applicants note that the Johnson et al (1999) paper is directed to RSV whereas but the present application teaches that some corticosteroids have been found not particularly useful for treating inflammation due to RSV when systemically administered (see, for example, the reported ineffectiveness of systemically administered prednisolone in infant RSV, in Bulow et al, Prednisolone treatment of Respiratory Syncytial Virus Infection: a randomized controlled trial of 147 infants, *Pediatrics*, **104** (6 December 1999), p e77), cited at page 14 of the application).

Conversely, Applicants teach that the use of such agents in conjunction with an authentic anti-viral (i.e., anti-RSV) antibody, such as a neutralizing antibody, including high affinity antibodies, such as those disclosed in the application, provides an effective method of treating respiratory infections (see the results provided by Figure 1 and the disclosure at page 14, lines 6-20, of the application).

If the art teaches away from systemic administration of anti-inflammatory agents in treatment of RSV, then there would be no reason to expect that combining such systemic treatment with systemic administration of the anti-RSV antibody of Johnson et al (1999) would provide a useful treatment technology, absent the teaching, and data, of the application.

As a final matter, Applicants note that because the obviousness argument is

made only against claim 35, and because Johnson et al (1999) fails to disclose systemic administration of the combination regimen while Prince (the '540) fails to disclose systemic administration of the anti-inflammatory component (only disclosing topical administration thereof), the claims should now all be in condition for allowance.

In view of the foregoing, Applicants believe that the grounds of rejection have been overcome and respectfully request that the Examiner reconsider the pending claims.

Applicant have enclosed herewith a request for a 2 month extension of time to respond, along with the fee paid by check. If any additional fee is due, the Commissioner is authorized to charge any and all such fees to Deposit Account No. 03-0678.

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Respectfully submitted,

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